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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,642	12/22/2000	Thomas B. Albrecht	026.00041	4973

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EXAMINER
LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/748,642	ALBRECHT ET AL.	
	Examin r	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-12,14-16 and 18* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-9, 14-16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

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DETAILED ACTION

Drawings

The corrected or substitute drawings were received on April 28, 2003. These drawings are accepted.

Election/Restrictions

This application contains claims 2-4 and 10-12 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 102

The rejection of record of claims 1, 5, 6 and 7 under 35 U.S.C. 102(e) as being anticipated by Potter et al. (US Patent No. 6,294,518) is withdrawn in response to Applicant's amendments.

The rejection of record of claims 1, 5, 9, 13 and 17 under 35 U.S.C. 102(b) as being anticipated by Gordon et al. (reference 5 on PTO form 1449, filed July 19, 2002) is withdrawn in response to Applicant's amendments.

The rejection of record of claims 1, 6-9 and 14-16 under 35 U.S.C. 102(b) as being anticipated by Henkart et al. (reference 2 on PTO form 1449, filed July 19, 2002) is withdrawn in response to Applicant's amendments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1 and 9 are maintained as rejected under 35 U.S.C. 102(e) as being anticipated by Roizman et al.

Roizman et al. disclose methods of inhibiting the replication of a virus, including herpes simplex virus and human cytomegalovirus, by administering an inhibitor of a viral protease.

Therefore, claims 1 and 9 are anticipated by Roizman et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is indefinite because it depends from a cancelled claim and, therefore, the limitations of claim 18 cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-9 and 14-16 are maintained as rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting viral replication using protease inhibitors disclosed in the art, does not reasonably provide enablement for generally inhibiting viral replication in any cell in any setting using generally any protease inhibitor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance

presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Claims 1, 6-9, 14-16 are drawn broadly to inhibiting the replication of generally any DNA virus and treating generally any DNA viral infection in an individual by inhibiting the activity of a cellular protease.

The specification discloses methods wherein the calpain inhibitors E64d and Z-Leu-Leu-H are administered to HCMV infected cells in vitro, which results in an inhibition of the degradation of $p21^{cip1}$ in those cells relative to untreated HCMV infected cells. The specification does not provide any evidence that HCMV replication is inhibited by E64d or Z-Leu-Leu-H, in vivo or in vitro, nor does it provide any evidence that administering E64d or Z-Leu-Leu-H to a subject treats a viral infection in said subject. The prior art discloses methods which are enabled, that fall within the scope of the claimed methods, however, such methods are a very small scope of the claimed methods, and would not enable the full scope of methods claimed. The prior art also discloses methods wherein protease inhibitors are administered to treat viral infections, and comprise the steps of the claimed methods and would inherently have any treatment effect as the claimed methods, however, these methods are only enabled to the same extent as the claimed methods and do not provide the guidance required to practice the methods over the full scope claimed.

At the time of the instant invention, and even to date, methods of treatment for viral infections were unpredictable, and the life cycle of many viruses were unknown or not well defined. The art of the field of viral infections did not provide sufficient

information to know what viruses require cellular proteases for replication, or what particular proteases a particular virus uses. The specification does not provide guidance by which the skilled artisan would know what protease to inhibit for particular viral infections, or replication of a particular virus. Even for the specifically claimed embodiment of calpain inhibitors, the art demonstrates that inhibition of calpain does not necessarily cause inhibition of replication. For example, Debaisi et al. (reference 8 on PTO form 1449, filed July 19, 2002) demonstrates that calpain inhibitors act independent of reovirus replication (see abstract, for example). Additionally, Debaisi et al. disclose that calpain may be involved in many physiological roles in a viral infected cell, but that further research would be required before a potential therapeutic intervention can be developed (see for example, p 699). The instant specification does not provide sufficient information regarding the very broad scope of viral infections encompassed by the claims, such that the skilled artisan would be able to practice the full scope claimed. In order to practice the scope of the claimed methods, one skilled in the art would need to undergo undue trial and error experimentation to determine what viruses can be treated using a particular protease inhibitor and how to treat such a viral infection in an individual. Given the complex nature of viral infections, and the difficulty in determining effective treatments, even through this undue trial and error experimentation, the skilled artisan may never be successful.

Therefore, at the time of the instant invention, one skilled in the art would not have been able to practice the claimed invention over the full scope claimed without undue trial and error experimentation.

Response to Arguments

Applicants arguments filed April 28, 2003 have been fully considered but have not been found persuasive.

In response to the rejection of record of claims 1, 5, 9, 13 and 17 under 35 USC 102(e) as anticipated by Roizman et al., Applicant argues that Roizman et al. only discloses inhibition of viral proteases and not cellular proteases. This argument has been considered to the extent that it reads on the rejection of claims 1 and 9 as anticipated by Roizman et al. This has not been found to be persuasive because Roizman et al. disclose inhibition of a viral protease produced in the cell and, therefore, is encompassed in the term "cellular protease".

In response to the rejection of record of claims 1, 5-9 and 13-17 under 35 USC 112, first paragraph, Applicant argues the claimed subject matter is fully enabled. Applicant argues that if the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim the enablement requirement is satisfied. Applicant argues that the skilled artisan could contact cells with a DNA virus contact infected cells with the inhibitor and determine if replication were inhibited. Applicant argues that the specification demonstrates that cells are infected with a DNA virus. Applicant argues that treating infected cells with protease inhibitors and measuring viral replication and assessing inhibition of replication, the unpredictability of the mechanism of inhibition notwithstanding. Applicant argues that measurement of levels or activity of the

preferred embodiment, calpain was well known. Applicant argues that prior art is available that teaches the skilled artisan how to infect cells and measure viral replication.

These arguments have been considered but not found to be persuasive. The specification does not provide methods that correlate reasonably with the full scope of the claimed methods. For example, the specification only provides in vitro (cell culture) examples and only provides methods using one type of DNA virus (HCMV) and two particular protease inhibitors (E64d and Z-Leu-Leu-H) inhibiting one cellular protease. These do not correlate with the broad scope of the claimed methods, which include in vitro treatment methods and inhibition of generally any DNA virus replication, using generally any protease inhibitor. The methods claimed are much broader in scope than the methods provided in the specification. Further, although administration of protease inhibitors were known in the art and methods for measuring viral replication were known, these arguments do not address the methods claimed. For example, the methods claimed are not directed to measuring the level of viral replication, rather to inhibition of viral replication. Being able to measure the potential outcome, or lack thereof, of a method does not enable the method. Determining viral levels does not address in vivo methods of treatment, as encompassed in the claims. Further, the methods of assessing replication discussed by Applicant do not even address the scope of the methods, which are directed to encompass a very broad range of viruses and protease inhibitors and include in vivo methods and therapeutic outcomes. These

methods are unpredictable, as discussed in the rejection of record, and the specification has not enabled the full scope of these methods.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached on Monday-Thursday 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

308-4242 for regular communications and (703) 305-1935 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
July 7, 2003

KAREN LACOURCIERE
PATENT EXAMINER